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CENTER FOR THE STUDY OF TRAUMATIC ENCEPHALOPATHY NEUROPATHOLOGY REPORT

PATIENT'S NAME: David Duerson
AUTOPSY#: SLI-67
DATE OF DEATH: 2/17/2011
DATE OF AUTOPSY: 2/18/2011
DATE BRAIN RECEIVED: 2/23/11
FROM: Dade County, FL
TYPE OF SPECIMEN: Fixed brain
Brain weight: 1300 grams

GROSS EXAMINATION
(Numerical score of severity key: 0 = none, 1+ = mild, 2+ = moderate, 3+ = severe, 4+ = very severe)

The meninges are thickened and fibrotic, there is scarring over the base of the brain
The cranial nerves (I-XII):
Olfactory bubs: unremarkable
The cerebral blood vessels:
Atherosclerosis of cerebral vessels: 1+ mid-Basilar, without occlusion
Obstruction of cerebral vessels: none

Parenchymal vascular lesions: none
Infarct(s) (>1.0 cm in diameter): none
Lacunes (<1.0 cm): none
Hemorrhages (parenchymal): none

There are no contusions. There is no atrophy of the cerebral cortex or prominent asymmetry.
The cerebral hemispheres are sectioned coronally, the brainstem is sectioned transversely and cerebellum is sectioned sagittally. The findings are:

Cavum septum anterior 0.5 cm, fenestrations: none

Ventricular size:
- Lateral ventricles:
  - Frontal horn: unremarkable
  - Occipital horn: unremarkable
  - Temporal horn: unremarkable
- Third ventricle: dilated, diamond shape posteriorly
- Fourth ventricle: unremarkable
- Cerebral aqueduct: unremarkable

Coronal sections of cerebrum:
- Hippocampal formation: unremarkable
- Amygdala: unremarkable
- Entorhinal cortex: unremarkable
- Striatum:
  - Caudate/Putamen: unremarkable
  - Globus pallidus: unremarkable
- Hypothalamus: unremarkable
- Mammillary bodies: unremarkable
- Thalamus: concave medial profile
- Subthalamic nucleus: unremarkable

Cerebral White Matter:
- The cerebral white matter is notable for prominent cribriform state in temporal and superior parietal subcortical white matter

Brainstem:
- Substantia nigra: white matter
- Locus coeruleus: white matter

Cerebellum: unremarkable

Other non-vascular gross CNS: none

MICROSCOPIC EXAMINATION

Available for microscopic examination are sections from representative regions listed below. The sections have been stained with Luxol fast blue, hematoxylin and eosin (LHE), and with Bielschowsky silver.

Additional staining methods have been used as follows:

AT8: 1,2,3,4, 5, 7, 8,10,11,12, 14,16A, 16, 18, 22, 25:
Alpha-synuclein: 1,2,4,5,7, 10,11,14
Amyloid beta: 4,7,10,11,14,18, 25
AlphaBcrystallin: 3, 11, 22
TDP-43: 11,14, 22
Ubiquitin: 3, 22

Key sheet of available sections

1. Olfactory bulb
2. Midbrain at level of red nucleus
2A. Midbrain at superior cerebellar peduncle
3. Precentral, postcentral cortex (BA 4,3,2,1)
4. Inferior parietal cortex (BA 39,40)
5. Anterior cingulate (BA 24)
5A. Superior frontal (BA 8,9)
6. Inferior frontal cortex (BA 10,11,12)
7. Dorosolateral frontal (BA45,46)
8A. Caudate, putamen, and accumbens (CAP) with septal cortex, fornix
8B. Insular cortex
9. Anterior temporal (BA 38)
10. Superior temporal (BA 20, 21,22)
11. Amygdala, with entorhinal cortex (BA 28)
12. Globus pallidus, insula, sub. innominata
13. Anterior hippocampus
14. Hippocampal formation, lateral geniculate
15. Superior temporal posterior (BA 41,42)
16. Thalamus with subthalamic nucleus
16A Thalamus with mammillary body
17. Posterior cingulate (BA23,31)
18. Calcarine cortex (BA 17,18)
19. Superior parietal cortex (BA 7B)
20. Upper pons (level of locus cœruleus)
20A. Lower pons at Vth cranial nerve
21. Medulla oblongata(including inferior olives)
22-1. Cervical spinal cord
22-2,3 Thoracic spinal cord
22-4, 5 Lumbar spinal cord
22-6 Sacral spinal cord
23. Cerebellar vermis
24. Cerebellum with dentate nucleus
25. Parastriate cortex

MICROSCOPIC FINDINGS

I. Leptomeninges:
Fibrosis: 1+

II. Cranial Nerves
Olfactory bulbs:
NFTs: 2+ at8
NTs: 2+
Lewy Bodies: none
Lewy neurites: none

III. Cerebral Blood Vessels:
Arteriolosclerosis: 1+
Amyloid angiopathy:
leptomeninges: none
intraparenchymal: none

IV. Cerebral cortex:

Cytoarchitecture (radial and laminar): normal
Neuronal loss: none
Spongiform change: none
NFTs: (AT8)
Rolandic: rare
Cingulate: 1+ NFT cingulate, gliosis, 3+ at8 periventricular region, fornix, induseum griseum
Insula: 4+ NFT
Septal: 4+ NFT
Inferior orbital frontal: 4+ NFT
Dorsolateral frontal: 4+ NFT
Inferior parietal: 2+, isolated
Temporal isocortex: 4+ NFT
Calcarine: none
Parastriate:
Distribution of NFTs:
Glial NFTs: 3+
White matter NFT and neurites: 3+
Perivascular collections: 3+
Patchy distribution depth of sulcus: 4+
Subpial glial NFTs: 3+
Superficial layers NFTs: 4+
Aß/Bielschowsky
SPs: (diffuse): none
SPs: (neuritic): none
Neuropil threads, dot like, threadlike: 4+
Microinfarcts: none
Lewy bodies: none

Hippocampal formation:
Neuronal loss (CA1): none
NFTs@200X: count CA1: 2+
Dentate: 1+ neurites
CA4: 3+
CA2: 3+
SPs: none
Hippocampal sclerosis: none
Hippocampal ferruginization: none
Microinfarcts: none
Lewy bodies, CA1, synuclein: none
Synuclein positive neurites in CA2/3: none

Entorhinal cortex:
Neuronal loss: 1+
Astrocytosis: 1+
NFTs layer 4/5 @ 200X: 4+
SPs; layer 4/5@ 100X; neuritic: none
Lewy bodies: none

Transentorhinal: 1-2+
Cerebral white matter:
Rolandic:
Loss of myelinated nerve fibers: 1+
Arteriolosclerosis: 1+
Microinfarcts: none
Perivascular macrophages: 3+
Cribriform state: none
Inferior parietal:
Loss of myelinated nerve fibers: 1+
Arteriolosclerosis: 2+
Microinfarcts: none
Perivascular macrophages: 2+

- Cribriform state: none

Dorsolateral frontal:
Loss of myelinated nerve fibers: 1+
Arteriolosclerosis: 1+
Microinfarcts: none
Perivascular macrophages: 2+
Cribriform state: none

Temporal isocortex and Extreme/external capsule:
Arteriolosclerosis: 1+
Microinfarcts: none
Perivascular macrophages: 3+
Cribriform state: 2+

Parastriate:
Loss of myelinated nerve fibers: 1+
Arteriolosclerosis: 1+
Microinfarcts: none
Perivascular macrophages: 3+
Cribriform state: none

V. Subcortical Nuclei:
Amygdala:
Neuronal loss: 1+
Astrocytosis: 1+
NFTs: 4+
SPs: none
Lewy bodies: none
Alpha-synuclein positive neurites: none
Substantia innominata (nuc basalis Meynert):
Neuronal loss: 1+
NFTs: 4+
Lewy bodies: none
Caudate/ Putamen
Cribriform state: none
Microinfarcts: none
Arteriolosclerosis: none
NFTs: 3+ accumbens only
Globus pallidus : unremarkable
Thalamus:
Microinfarcts: none
Astrocytosis: none
NFTs: 2+
Hypothalamus:
NFTs: 4+
Mammillary bodies:
NFTs: 2+

VI. Brainstem
Periventricular aqueductal gray: 1+ AT8
Gliosis: 3+ periaqueductal region
Superior colliculus:
glial NFTs: 1+
Substantia nigra, pars compacta:
Neuronal loss: 1+
Astrocytosis: none
Extraneuronal pigment: 1+
Lewy bodies: none
Lewy neurites: none
Pale bodies: none
Spheroids: none
NFTs: 3+
Microinfarcts: none

- pars reticulata: none
  cerebral peduncle: none

Dorsal and median raphe:
Neuronal loss: 1+
NFTs: 4+
Lewy bodies: 1+
Midbrain reticular formation: 1-2+ AT8
Locus coeruleus:
Neuronal loss: 1+
NFTs: 4+
Lewy bodies: none
Basis pontis:
NFTs: rare
Dorsal nucleus of the vagus:
Lewy bodies: none
NFTs: 1-2+
Inferior olives:
Neuronal loss. none
NFTs: none
Pyramid: unremarkable

VII. Cerebellum:
Cortex: unremarkable
Dentate nucleus: unremarkable
Purkinje cells:
Neuronal loss: 1+
White matter: unremarkable

VII: Spinal cord:
Cervical:
Tau immunoreactive neurites: 1+
NFTs: none
Anterior horn cell loss: none
Corticospinal tract degeneration: none

DIAGNOSES:

1. Chronic Traumatic Encephalopathy: Stage III/IV with classic pattern of neurofibrillary tau pathology involving frontal, temporal and insular cortices, subcortical white matter, hypothalamus, thalamus, mammillary bodies, substantia nigra, median raphe, locus coeruleus. TDP-43 neurites are primarily limited to the lateral midbrain in a region characterized by marked glial tangles. There is no evidence of Alzheimer's disease, there is no beta amyloid protein deposition, and there is no amyloid angiopathy. A few alpha-synuclein positive Lewy bodies are found in the olfactory bulb and median raphe. The white matter is notable for myelinated fiber loss, axonopathy especially prominent around blood vessels and thickened small arterioles with abundant hemosiderin-laden perivascular macrophages.

NEUROPATHOLOGIST:

Ann C. McKee, MD